REMARKS

This Amendment is submitted in response to a non-final Office Action mailed on May 12, 2009. Claims 12-26 are currently pending with claims 21-26 being withdrawn in view of the previous Restriction Requirement. Claims 12-14 and 18 stand rejected under 35 U.S.C. §102(b), and claims 15-17 and 19-20 stand rejected under 35 U.S.C. §103(a). An additional request to correct the specification to include Seq. ID. Nos. and a sequence listing has also been made. In response, Applicants amend the specification to correct the Seq. ID issue, file a sequence listing and computer readable form (CRF), and submit a statement that Sequence Listing and CRF are identical. In regard to the rejections, Applicants respectfully traverse by argument. The Commissioner is hereby authorized to charge deposit account 02-1818 for any fees which are due and owing.

In the Office Action, the Patent Office asserts that the present application fails to comply with the sequence listing requirements pursuant to 37 CFR 1.821-1.825. In particular, the Patent Office notes that no Sequence Listing has been filed and that several sections of the specification contain sequences without corresponding SEQ ID NOs. In response, corrections to the specifications have been made as required by the Office Action. Specifically, the phrases "sequence no. #" have been corrected to read "SEQ ID NO: #." Furthermore, Applicants submit herewith the required Sequence Listing Statement along with the paper copy of the sequence listing and the computer readable form of the sequence listing. Applicants further submit that the substitute sequence listing does not introduce any prohibited new matter.

In the Office Action, claims 12-14 and 18 stand rejected under 35 U.S.C. §102(b) as anticipated by Yoshimoto, et. al. *JACS*, **125**, 8982-83 (July 4, 2003.) Independent claim 12 claims a method for detecting a gene mutation comprising forming a double-stranded nucleic acid from i) a single stranded target nucleic acid having a target base compound and two partial sequences with the target base there between, and ii) two single-stranded detecting nucleic acids complementary to the two partial sequences. In applying the disclosure of Yoshimoto to claim 1, the Patent Office asserts that the element i) above is met by the strand on the left side of Figure 1, and that element ii) is met by the strand containing the AP site. Applicants respectfully disagree.

The claim language requires that the double-stranded nucleic acid form using two single-stranded nucleic acids. Yoshimoto only contains one strand. Specifically, Yoshimoto has a single strand of DNA in which one of the bases has been replaced by an abasic site - a tetrahydrofuranyl group. Yoshimoto discloses that "figure 1, an AP site-containing DNA **strand** is hybridized with a normal DNA strand so as to place the AP site opposite." Yoshimoto, p 8982, second paragraph, lines 4-5 (emphasis added.) Note that Yoshimoto recognizes this is a single strand. Also, "In this study, a tetraydrofuranyl residue (dSpacer) which lacks a nucleobase moiety is utilized for the design of an AP site and is incorporated with 11-mer oligonucleotide (5'-TCCAGXGCAAC-3', X-dSpacer.)." *Id.*, lines 11-15. Here, note that Yoshimoto describes the molecule as an 11-mer, not two 5-mer oligonucleotides. Clearly, this designates a single-strand nucleic acid in Yoshimoto. In contrast, the claimed invention does not utilize a single-stranded DNA containing an abasic site. Instead, the claimed invention uses two single stranded nucleic acids complementary to the partial sequences on the target nucleic acid. The resulting double stranded nucleic acid then has a gap that the incoming receptor can insert into.

The Patent Office appears to be asserting that the single strand in Yoshimoto can be interpreted to be two single strands 2a and 2b. However, this interpretation goes against the disclosure in Yoshimoto and the language of those skilled in the art. Yoshimoto clearly describes the molecule as a strand, as discussed above. Moreover, one skilled in the art would refer to these pieces, designated 2a and 2b by the Patent Office, as the fragments or sections of a strand. In fact, the Patent Office's own language makes this clear. The Patent Office denotes stand 2a as the "top half" and strand 2b as the "bottom half." This terminology begs the question, "Top and bottom halves of what?" The answer is obviously "a whole single strand."

This difference is not insignificant. Preparation of the single stranded molecule in Yoshimoto having the dSpacer requires chemical synthesis of that spacer into the backbone of the single strand. This chemical synthesis adds additional costs and inconvenience to the preparation of the molecule, as discussed in paragraph [0010] of Applicants specification. Moreover, the difference in kinetics and thermodynamics of hybridizing two single strands versus a single strand with two complementary shorter strands should not be ignored. Finally, if two single-strand nucleic acids were interpreted as a two fragments linked by spacer, then instant

claim 17 becomes problematic because the two single-strand detecting nucleic acids could not be added separately if they were tethered together.

Finally, the language of the claim should make clear that a partial sequence, such as the Examiner is asserting, is not the same as a single strand. Specifically, Applicants describe in i) the single-strand target nucleic acid as having two partial sequences with the target base therebetween. This is effectively what the Examiner is describing – two partial strands connected by a dSpacer. Then, Applicants describe in ii) two single strand nucleic acids. These strands are not defined as connected, are plural, and are not described as "partials." They are each independent from one another. A review of the specification and the other claims should make that distinction clear.

In summary, the Patent Office's assertion that the single-strand nucleic acid of Yoshimoto meets the limitation of two single-strand nucleic acids is improper because it goes against the clear language of the specification and claims, the clear discussion within Yoshimoto, and the clear understanding of one of ordinary skill in the art.

In the Office Action, claims 15-17 and 19-20 are rejected under §103(a) as unpatentable over, Yoshimoto in view of Nakatani *et al.*, *JACS*, **123**, 12650-57 (2001). In the rejections, the Patent Office relies on Yoshimoto for the elements present in independent claim 12, and relies Nakatani for the limitations present in claims 15-17 and 19-20, all of which depend from claim 12. Because Nakatani does not remedy the deficiency in Yoshimoto of two single-strand detecting nucleic acids, the rejection under §103(a) is improper and should be withdrawn.

For the reasons set forth above, Applicants assert that claims 12-20 are novel and non-obvious of the cited prior art. Applicants request that the rejections be withdrawn, that the application is now in condition for allowance, and respectfully request consideration of the same.

Respectfully submitted,

K&L GATES LLP

BY _____

Thomas C. Basso
Reg. No. 46,541
Customer No. 24573

Dated: August 12, 2009

Notice to Comply	Application No. 10599101	Applicant(s) TERAMAE ET AL.	
	Examiner SUCHIRA PANDE	Art Unit 1637	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application.**

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571) 272-0731 or (571) 272-0951
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/Suchira Pande/ **Examiner, Art Unit 1637**	